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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,505	06/05/2006	Mei Wang	1328-28	2905

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EXAMINER	
GITOMER, RALPH J	
ART UNIT	PAPER NUMBER
1657	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,505	WANG ET AL.	
	Examiner	Art Unit	
	RALPH GITOMER	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-20 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18-20 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/10/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment and Declaration received 4/12/11 and the IDS's received 10/22/10 and 3/10/11 have been entered and claims 1-16, 18-20, 25 are currently pending in this application.

The elected specie is biomarkers. Again, please inform the examiner of all related applications, pending, allowed or abandoned, and their status.

The point of novelty considered here is employing multivariate analysis which is interpreted to mean analyzing data from more than one variable or in this case measurement as related to biological effect of a multicomponent mixture. The preamble of the claims are directed to determining if a synergistic effect is present but the method steps presume such an effect is present. The claims lack any multivariate analysis.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16, 18-20, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Huyn, Borisy, Afeyan, Khwaja, Pugh.

Huyn (2002/0095260) entitled “Methods for Efficiently Mining Broad Data Sets for Biological Markers” teaches in the abstract, determining measurements from blood samples of biomarkers for assessing response to a drug. In column 1 first paragraph, various statistical methods of interpreting data is discussed.

Borisy (2003/0096309) entitled “Screening System for Identifying Drug-Drug Interactions and Methods of Use Thereof” teaches in paragraph 20 providing a drug library , determining the results of administration, and identifying drug combinations that provide the desired result. In paragraph 48 a number of drugs may be tested in different combinations. In paragraph 52 profiling the combinations is discussed.

Afeyan (2005/0283320) entitled "Method and System for Profiling Biological Systems” teaches in paragraph 8 profiling a biological system for pharmacological agent response. In paragraph 11 multivariate analysis on a plurality of data sets is shown.

Khwaja (6,379,714) entitled “Pharmaceutical Grade Botanical Drugs” teaches in column 3 last paragraph, a plant extract may contain a plurality of active ingredients which exhibit a given biological activity. An aliquot is removed, separate the aliquot into a plurality of marker fractions each of which include an ingredient and the degree of biological activity for each of the marker fractions is determined. In column 4 first paragraph the invention is useful for determining if a particular botanical material meets

levels of pharmacological activity. In column 7 last paragraph, biological assay include cell proliferation assays.

Pugh (J Agricultural Food Chem) entitled "Characterization of Aloeride, A New High MW Polysaccharide from Aloe vera With Potent Immunostimulatory Activity" teaches on page 1031 isolated fractions of aloe were tested in a macrophage assay. On page 1033 Fig. 3 shows a dose response for a fraction.

The claims may differ from the above references in that they specify multivariate analysis specifically and various to separate the components of the product and various types of biological profiles.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ multivariate analysis in the methods of analysis shown by each of the above references because each reference teaches analyzing data from more than one measurement. Employing known methods to separate chemical mixtures into single compounds with the expected results would have been obvious. And the claimed biological profiles are conventional in this art.

The nature of pharmacognosy is such that most all drugs originated in natural products which are mostly a mixture of compounds and the desired activity was found in some fashion to be associated with a specific and single chemical which was then isolated or synthesized. In other cases, such as in the references above, synergy between components was investigated. The present claims read on this old method. And to vary the concentrations of components does not lend patentability, dose response curves to LD50 are conventional tools of investigation in this art.

Applicant's arguments filed 4/12/11 have been fully considered but they are not persuasive.

Applicants response argues that the claims have been amended to identify a synergistic effect on the biological profile of a disease and the product mixture as well as the biological profile used in the analysis. Other approaches use a single disease marker for a disease evaluation whereas the present invention applies multifactorial disease patterns. Standard drug screening is directed to a single compound at a time is tested whereas the present invention employs multiple components seeking synergistic effects and provides measurements at a systems level which is important for multifactorial disease, not at a molecular or cellular level.

Huyn does not measure the effect of a complex mixture on a complex disease pattern or identify its bioactive profile but merely seeks relevant biomarkers. Borisy employs synthesized or purified components to identify combinations of known drugs. Borisy does not obtain information regarding feedback signaling. Afeyan does not teach varying the concentrations of one or more components to determine the respective concentrations required for the desired effect on a disease. Khwaja focuses on isolating compounds which will not find synergism. Pugh isolates compounds and does not seek synergism. Traditional pharmacognosy isolates compounds to find an active compound whereas the present invention finds bioactive compound profiles that work in synergy using a disease pattern.

It is the examiner's position that the invention as described in the arguments is not enabled. No synergy is seen in the specification or claims. Huyn measures biomarkers to assess drug response using statistical methods. Varying the dose of the drug would affect the response. The claims are directed to a natural product mixture which would include synthesized or purified components. No feedback signaling is claimed. Afeyan profiles biological systems where the dose of a drug tested would affect its response. Regarding Khwaja and Pugh, the claims are not directed to synergism. Neither the method claimed nor any teachings found in the specification as originally filed teach one of skill in this art how to determine which components or concentration of a complex mixture of components provide synergy with other components. Employing multiple markers of a disease is not claimed, see present claim 1(b) directed to "determining said synergistic effect of a series of samples of the multicomponent mixture on the biological profile of the disease."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 18-20, 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A reading of the specification reveals the point of novelty may reside in employing multivariate analysis in an interactive fashion to improve a natural product mixture by examining a biomarker. The specification reveals no natural products, no improvements and no multivariate analysis. And what biomarker may be intended is unclear.

The claimed method has been amended to read determining a synergetic effect rather than an impact. The present specification states at the top of page 7 “The determination of biological effects and in particular synergetic multicomponent effects in accordance with the present invention is illustrated by the example of herbal medicine products in intervention strategies.” Irrespective of the meaning of this statement, the specification does not teach one of skill in this art how to make and use such a method. The teachings appear to be directed to determining an effect caused by multicomponent mixtures, no synergy is seen in any form or calculated related to the components in the mixtures or their relative concentrations. The example on page 18 seeks a biological response and no issues related to synergy are seen. It is noted that synergy of complex mixtures upon diseases is not simple and is unusual in general.

Applicant's arguments filed 4/12/11 have been fully considered but they are not persuasive.

Applicants response argues that the specification describes the claimed method steps sufficient to practice the invention and actual reduction to practice is not required. A Declaration is presented where synergistic compounds were tested.

It is the examiner's position that the specification does not teach the claimed invention in such a fashion that one of skill in this art could practice the invention. Referring to the single prophetic example in the specification, batches of herbal mixtures are administered to an animal model or a human trial, a control is mentioned. Endpoints are measured. But this is entirely hypothetical and to subject, disease, biomarker or multivariate analysis is shown. What are the biomarkers for which diseases? What analysis is performed? What improved natural product is shown? The issue is not reduction to practice but how to actually perform the desired method and obtain a useful result which is not found in the specification as originally filed.

The Declaration shows a method that is not enabled by the specification and is not claimed. Further, the Declaration discloses identity of the components found in the extract but no data regarding a biological profile or synergy or multivariate analysis is seen.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16, 18-20, 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/571,087. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '087 are directed to determining an impact whereas the present claims are directed to determining a synergetic effect, both by the same method steps.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The above rejection is maintained.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tallarida teaches conventional multivariate math of synergy.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ralph Gitomer/
Primary Examiner, Art Unit 1657

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